C Unit 3 C{PRIVATE }

Basic Toxicological Principles

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3.1 INTRODUCTION

Hazardous waste sites pose a multitude of health and safety concerns, any one of which could result in serious injury or death. Several factors distinguish the hazardous waste site environment from other occupational situations involving hazardous substances. Improper control of chemical substances can pose a severe threat to site workers and the general public. Preventing exposure to toxic chemicals is a primary concern at a hazardous waste site. Most sites have a variety of chemical substances in gaseous, liquid, or solid form, which may enter the body by inhalation, skin absorption, ingestion, and through puncture wounds. If each person learns about proper protection against exposure and practices preventive measures, the body will be able to defend itself and the person will be safe on the job.

3.2 DEFINITIONS

The following definitions will help you understand toxicological principles.

1. **Poison**CAny substance that has a negative effect (illness or death) when ingested, inhaled, or absorbed in relatively small quantities.

2. **Toxicology**CThe study of the harmful effects of chemicals on living things, especially humans. More specifically, a study of poisons and their effects on the body.

3. **Hazardous Materials**CThose materials that pose an unacceptable risk to humans, property, or the environment when released from their containers. These chemicals may be flammable, reactive, corrosive, or toxic. These properties are listed on the Material Safety Data Sheet (MSDS) for each given substance.

4. **Dose**CThe amount of a substance that enters the body, usually expressed as milligram of substance per kilogram of body weight of the exposed individual (mg/kg).

5. **Threshold Limit Value (TLV)**CTLV refers to airborne concentrations of substances and represents conditions under which almost all workers may be repeatedly exposed without adverse effects. It is used to designate safe exposure limits by the American Conference of

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Governmental and Industrial Hygienists (ACGIH).

6. **Threshold Limit Value Time-Weighted Average (TLV-TWA)**CThe time-weighted average concentration for a normal 8-hour workday and 40-hour work week, to which nearly all workers may be repeatedly exposed without adverse effect (set by ACGIH). For example, a worker exposed to 200 ppm of a substance for four hours and 0 ppm for the other four hours of the shift has had an eight-hour time-weighted average exposure of 100 ppm. If the TLV-TWA for the chemical is less than 100 ppm, then the exposure exceeded the limit.

7. **Threshold Limit Value Short-Term Exposure Level (TLV-STEL)**CThe exposure level safe to work in for short periods of time (15 minutes), 4 times a day maximum, with at least 60 minutes between exposures. It should not be exceeded at any time during the work day (set by ACGIH).

8. **Threshold Limit Value Ceiling (TLV-C)**CThe concentration that should not be exceeded, even for an instant. This value has been established as the maximum level to be used in computing the TWA and STEL limits (set by ACGIH).

9. **Immediately Dangerous to Life and Health (IDLH)**CThe maximum level from which a worker could escape without any impairing symptoms or any irreversible health effects (designated by the National Institute of Occupational Safety and HealthCNIOSH).

10. **Lethal Dose**CThe amount of a substance that kills the exposed population.

11. **Lethal Dose-50% (LD 50)**CThe dose of a substance that causes death in 50% of the exposed population of test animals (rats, mice, or rabbits).

12. **Effective Dose-50 (ED-50)**CThe statistical estimate of the dose of a substance that causes a measured effect in 50% of a population of animals.

13. **Permissible Exposure Limit (PEL)**CTime-weighted average and ceiling concentrations similar to (and in many

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cases derived from) the threshold limit values (TLV, published by ACGIH). NIOSH establishes the Recommended Exposure Limits (REL), then OSHA establishes the Permissible Exposure Limits (PEL) as enforceable regulations.

3.3 DOSE/RESPONSE RELATIONSHIPS AND EXPOSURE LIMITS

The principle that a larger dose will cause a more significant response is called the dose/response relationship. Note that there may be no significant response if the dose is small enough. There are three factors that determine the severity of the toxic response to a chemical. These are dose, time, and toxicity of the substance. The greater the toxicity, the lower the dose it takes to produce a toxic effect.

It is important to remember that every substance has the potential to be toxic, and that it is only the dose that makes it a poison.

! **Example:** A quart of alcohol consumed over a year's time would have little to no effect on a person, but to drink the entire amount in a very short period of time would cause serious illness or even death. This example shows the importance of time in any dose/response relationship. To obtain an effect from a substance you need several things: a sufficient amount of a substance, a way to get the material into the body, and a limited period of time.

In the workplace, the amount of a substance that an employee is exposed to is limited by OSHA through standards called Permissible Exposure Limits (PELs). Advisory limits published by NIOSH and ACGIH are called Recommended Exposure Limits (RELs) and Threshold Limit Values (TLVs), respectively. After the presence and concentrations of specific chemicals or classes of chemicals have been established, the hazards associated with these chemicals must be determined. Refer to standard reference sources for data and guidelines on permissible levels of exposure, as set by ACGIH, OSHA, and NIOSH.

The TLV exposure limits are set by the ACGIH and are suggested levelsCnot enforceable limits. Some of the TLV limits are revised every year. The ACGIH feels the PEL limits were not protective enough due to industry influence on the committee members. These levels are only estimates of safe levels based on animal tests, and may be changed as more information about the toxic effects of chemicals on humans becomes available.

An extensive animal testing protocol would consist of: (1) biochemical studies on the metabolism, biotransformation and biochemical effects, (2) acute and short term toxicity effects, (3) special studies on reproduction, teratogenicity, mutagenicity, neurotoxicity, potentiation and carcinogenicity.

3.4 SENSITIVITY

Some people will have adverse health effects at levels well below the TLV. The fact that some people are hypersensitive to certain chemicals may be due to previous exposure to the chemical or different metabolic rates. Even within a population of the same species, there will be differences in sensitivity to the toxicity of chemicals. Factors affecting the sensitivity of an individual to chemicals include:

- genetic differences;
- sex and hormonal differences;
- nutritional and dietary factors and medications;
- age and maturity; and
- smoking.

3.4.1 GENETIC DIFFERENCES

Genetic variation in humans allows for the wide differences in susceptibility to toxic chemicals. The genetic makeup of an individual is expressed by the presence or absence of key enzymes used to process toxic chemicals in liver cells.

3.4.2 SEX AND HORMONAL DIFFERENCES

Sex and hormonal status appear to be factors in susceptibility to certain chemicals. In mice experiments, female mice show little response to chloroform exposures that are lethal for males. Yet female rats and rabbits are more susceptible to the toxic effects of parathion and benzene than males. Pregnancy has been shown to markedly increase the susceptibility of mice to some types of pesticides and similar effects have been reported for lactating animals exposed to heavy metals.

Hyperthyroidism and hyperinsulinism may also alter the susceptibility of animals, including humans, to toxic chemicals.

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3.4.3 NUTRITIONAL & DIETARY FACTORS ANDMEDICATIONS

Generally, people who lack essential minerals in their diet will absorb and retain these minerals readily along with an increased absorption of toxic metals such as cadmium and barium. A person on a low-calorie, low-protein diet is usually more sensitive to a number of toxic chemicals. Certain medications also increase a person's susceptibility to many toxic chemicals.

3.4.4 AGE AND MATURITY

Some chemicals are more toxic to infants and children than to adults. For example, lead ingestion has much more severe effects on the nervous systems of infants and children. Also, the very young are unable to metabolize and detoxify chemicals as well as adults. Elderly humans may be more susceptible to some toxic chemicals because the detoxifying capacity of the liver and the excretory capacity of the kidneys may decrease with age.

3.4.5 SMOKING

It is well documented that smoking causes lung cancer and other respiratory and cardiovascular diseases. In addition, smoking is synergistic with asbestos and other chemicals in causing more severe damage to the respiratory system.

Several thousand components have been identified in the gaseous and particulate substances in cigarette smoke. Carbon monoxide combines with hemoglobin in red blood cells to reduce the oxygen-carrying capacity of the blood. Also, cigarette smoke contains small amounts of toxic chemicals, especially acetaldehyde, acetone, and hydrogen cyanide. The tiny particles cause lung damage and form tobacco tar, which contains several carcinogenic (cancer-causing) agents. These carcinogenic particles include benzopyrene, nitrosamines, nickel compounds, phenols, and nicotine (the addictive portion of tobacco smoke).

3.5 TOXIC EXPOSURES TO THE BODY

3.5.1 ROUTES OF EXPOSURE

For a chemical to exert a toxic effect on an organism, it must first gain access to the cells and tissues of the organism. In humans, the major routes by which toxic chemicals enter the body are inhalation, ingestion, dermal (skin) absorption, and injection. The absorptive surfaces of the tissues of the gastrointestinal (digestive) tract, lungs, and skin all allow chemicals to move across them at different rates.

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3.5.1.1 Inhalation

Inhalation brings chemicals into contact with the lungs. Most inhaled chemicals are gases like carbon monoxide or vapors of volatile liquids like trichloroethylene. Absorption in the lungs is usually high because the surface area in the alveoli is large and blood vessels are close to the exposed surface. Gases cross the lung by diffusion, with the rate of absorption depending on the solubility of the toxic agent in blood.

Some chemicals that do not directly affect the lungs may pass through lung tissue into the bloodstream, where they are transported to other vulnerable areas of the body. When a sufficient dose of benzene is inhaled, it is carried via the blood to the bone marrow, where it may inhibit the manufacture of red blood cells. Other toxic chemicals may not be detected by human senses, that is, they are colorless, odorless, and may not produce immediate symptoms. Chemicals can also enter the respiratory tract via punctured eardrums and place a person at risk in certain workplaces.

Particulate substances may also be inhaled in solid or liquid form as dusts or aerosols. The lipid-soluble liquid aerosols readily cross cell membranes. The absorption of solid particles depends upon the size and chemical nature of the particles. Very small, insoluble particles may remain in the lung alveoli indefinitely. Larger particles are deposited in the mucus in the upper areas of the respiratory tract where they will be expelled by coughing and sneezing, or swallowed into the gastrointestinal tract.

3.5.1.2 Ingestion

Ingestion brings chemicals into contact with the tissues of the gastrointestinal tract. The normal function of the gastrointestinal tract is the digestion and absorption of foods and fluids. The stomach and intestines are effective in absorbing toxic chemicals that contaminate food and water, for example, cyanide. Accepted standard operating procedures forbid eating, drinking, chewing gum and tobacco at a hazardous waste site to prevent ingestion of toxic substances.

3.5.1.3 Skin and Eye Absorption

Some chemicals may cause skin and eye injury following direct contact or exposure. Some pass through the skin into the bloodstream, where

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they are transported to target organs. For example, when phenol is absorbed in large enough quantities, it is carried to the nervous system where it may cause loss of feeling, paralysis, or death. Skin absorption is enhanced by abrasions, cuts, heat, and moisture.

The eye is particularly vulnerable because airborne chemicals can dissolve in its moist surface and be carried to the rest of the body through the bloodstream.

Wearing protective equipment, not wearing contact lenses in contaminated atmospheres (since they may trap chemicals against the eye surface), keeping hands away from the face, and minimizing contact with liquid and solid chemicals can help protect against skin and eye contact.

3.5.1.4 Exposure by Penetration or Injection

The last primary route of chemical exposure is injection or penetration, in which chemicals are introduced into the body through puncture wounds (for example, by stepping or falling onto contaminated sharp objects). Wearing safety shoes, avoiding physical hazards, and taking common-sense precautions are important protective measures against injection.

3.5.2 SUSCEPTIBLE AREAS

The area most susceptible to toxic chemicals is the respiratory system because it has such a large area in the alveoli where chemicals can be absorbed directly into the blood stream. The surface area of the lungs is 45 times greater than that of the skin (90 square meters compared to 2 square meters).

3.5.3 DURATION AND FREQUENCY OF EXPOSURE

The toxicity of many chemicals depends on the length of time over which the exposure has occurred. First, some chemicals are not readily eliminated from the body, so that continued exposure to low doses (each too small to produce an observable effect) may lead to an accumulation of the chemical in the body at levels high enough to produce adverse results. For example, cadmium is usually retained in the body and tends to accumulate in the kidney until levels become high enough (usually after many years) to cause renal damage.

Secondly, toxic effects may depend on duration of exposure. When an injury to cells is not quickly repaired by the body's repair processes, the damage continues to build. Thus, a dose of a chemical that causes a limited, but irreversible damage may have no immediate apparent effect, but the result may be easily observed with continued exposure.

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Finally, some adverse effects simply require an extended period of time to develop, even though they might be the result of an exposure that occurred months or years earlier. For example, lead exposure may impair the development of the nervous and other systems in young children, even at low doses with a short period of exposure. Similarly, the development of tumors following high dose, long term exposure to carcinogens may take months or years to occur.

3.6 TOXIC EFFECTS

3.6.1 SEVERITY OF RESPONSE

A toxic chemical may produce harmful effects in a number of organs, but the severity of the response may be quite different depending on the inherent toxicity of the chemical, the length of time of the exposure, and the dose. The toxicity of a material is based on the toxic dose (TD), effective dose (ED), and lethal does (LD). Then the LD 50 (the lethal dose for 50% of the test group) may be determined. The lower the LD 50, the more toxic or lethal the material. See Figure 1 on the next page.

3.6.1.1 Acute Effect

An acute effect is one that can occur immediately after a single short-term exposure (less than 24 hours). The effect can be from mild to lethal and is usually reversible if it is not lethal. Acute effects and their causative agents are classified below.

- **Simple Asphyxiants**. Simple asphyxiation means that the body does not receive enough oxygen to operate properly and the person suffocates. Simple asphyxiation can occur if you enter a vessel or room that contains a gas, like carbon dioxide or nitrogen, that has displaced so much oxygen that there isn't enough left to maintain life.

- **Chemical Asphyxiants**. Carbon monoxide and cyanide are called chemical asphyxiants because exposure to high levels can prevent oxygen from being used by the body. The carbon monoxide in auto exhaust can cause chemical asphyxiation even when a normal quantity of oxygen is present in the air, since it prevents the body from using the oxygen.

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- **Anesthetics**. Anesthetics can cause impaired judgment, dizziness, drowsiness, headache, unconsciousness, and even death. They include substances such as alcohols, solvents, paint removers, and degreasers.

- **Neurotoxicants**. A neurotoxicant is a substance that has the potential for slowing or reducing the brain's ability to control the various parts of the body. Substances such as lead and mercury have been shown to be neurotoxic.

- **Irritants**. An irritant is a substance that can cause temporary discomfort or pain to the eyes, skin, or respiratory system. The tearing of the eyes caused by onions or the burning sensation in the nose caused by breathing ammonia are examples of irritant effects.

- **Corrosives**. Corrosives are substances, such as caustic soda, that have a severely damaging effect when they contact skin, eyes, or mucus membranes. Serious, sometimes permanent, damage can result; contact with eyes can cause loss of vision.

- **Allergens**. An allergic response is a toxic effect such as that caused by poison ivy or ragweed. The first exposure to a substance causes no reaction. However, following many exposures, or even a single exposure, the body's immune system undergoes a significant change. Then, with subsequent exposures, the person shows signs of an allergic response (rash and shock).

3.6.1.2 Subacute Effect

A subacute effect is one the may occur within five days after exposure. It can be mild or severe and is usually reversible.

3.6.1.3 Subchronic Effect

A subchronic effect occurs following several doses of the chemical over several days. The effect can be mild to severe but is usually not reversible, and may result in death.

3.6.1.4 Chronic Effect

A chronic effect can occur months or years after long-term exposure to low levels of toxic chemicals. In many cases, the condition is severe, irreversible, and may result in death. Chronic effects are produced by the following.

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- **Carcinogens**Csubstances that cause malignant tumors. Most chemicals labeled carcinogens cause cancer in animals. Vinyl chloride, benzene, and certain coal tar derivatives are known to cause cancer in humans.

- **Reproductive Toxicants**Csubstances that lower fertility and survivability of the fetus. Some reproductive toxicants include metals, chlorinated organics, and anesthetics. **Teratogens** are reproductive toxicants that cause abnormalities in fetuses during development in the uterus. These materials may be absorbed into a pregnant woman's body, travel via the bloodstream to the unborn child, and cause gross abnormalities, skeletal and visceral malformations, and even behavior changes. Chemical teratogenesis is usually the result of short-term exposure during a critical period of fetal development. Some teratogens are methyl mercury, lead compounds, alcohol, diethylstilbestrol (DES), thalidomide, and X-rays.

- **Mutagens**Csubstances that cause changes in the genetic makeup (DNA changes in the chromosomes) of cells. When these changes occur in egg and sperm cells, there may be alterations in the formation and function of the offspring.

  - Examples of human mutagens are mercury and lead compounds, benzopyrene, mustard gas, UV light, and X-rays.

- **Specific organ toxicants**Csubstances that cause an adverse effect on a specific organ of the body, for example, hepatotoxicants (liver damage), kidney toxicants, neurotoxicants (nervous system damage), and respiratory toxicants (lung damage). A known hepatotoxicant is carbon tetrachloride, a solvent that causes liver damage.

Refer to Table 1 for examples of hazardous waste chemicals and their effects.

3.6.2 LOCAL VS. SYSTEMIC TOXICITY

A local effect occurs when the toxic chemical causes damage to the

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local area where the chemical enters the body. For example, an acid or alkali burn to the eye, causing blindness.

A systemic or remote effect results from a substance entering the body by inhalation, skin absorption, ingestion, or penetration and causing an effect on an internal or remote system or organ. For example, phenol may be absorbed through the skin and cause loss of feeling, paralysis, or even death.

3.6.3 CHEMICAL INTERACTION

Many substances may act on the body simultaneously, causing the effects of each chemical to be different, either enhanced or diminished, as compared to the effects of that chemical alone. Thus mixtures of chemicals potentially could cause different effects than those caused by the single compounds. The effects of two or more chemicals may be **additive,** that is, the total effect is the sum of the two added together (2+3=5).

Two or more chemicals may work together to produce a **synergistic** or enhanced effect (2+2=15). Or, one chemical or circumstance may cause another chemical to cause more drastic damage than the second chemical alone (0+2=10); this is called **potentiation.** For example, smoking increases the lung damage produced by asbestos. **Antagonism** may occur when one chemical actually reduces the damage usually caused by another chemical (4+6=5), such as a base neutralizing an acid.

3.6.4 COURSE OF EXPOSURE

A substance may be absorbed into the body, distributed through the body, and excreted or cleared from the body in various ways depending on the route of exposure. See Figure 2 on the next page.

- When a chemical is inhaled (as a gas, aerosol, particle, dust, or fume), it enters the upper airways and lungs. It can then be absorbed into the blood and lymph and carried throughout the body.

- When a substance is ingested with food and liquids, it enters the gastrointestinal tract where it can be absorbed into the blood and lymph and enter the liver, kidneys, lungs, and all parts of the body.

- A chemical may enter the body by absorption through the skin or by a puncture wound (penetration), and be carried throughout the body by the blood and lymph systems.

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After the chemical has entered the circulatory system (blood and lymph), circulated and metabolized, it may be excreted or cleared from the body (clearance) by the expulsion of feces (bowel movement), via urine (urination), via expelled air (respiration), or via the body secretions (sweat). Chemicals vary widely in their rates of absorption, metabolism, distribution, and clearance from the body. Some are stored in the liver or fatty tissues for extended periods of time, where they may accumulate and cause extensive damage.

3.7 TOXICOLOGICAL EFFECTS ON THE HUMAN BODY

3.7.1 SURVEY OF BODY SYSTEMS, DEFENSES, AND DAMAGE

It must be noted that none of the body systems function alone. All the systems are interrelated, and damage to one system affects other areas of the body.

3.7.2 THE SKIN

The external surface of the skin is the epidermis, It is supported by the underlying dermis and subcutaneous fatty tissue. It is supplied with a waxy oil from the oil (sebaceous) glands for lubrication, and sweat (perspiration) from the sweat glands for cooling. In the dermis, there is a generous supply of nerves to sense heat, cold, touch, and pain; and blood vessels to supply nutrients to the cells.

The unbroken skin is a barrier between the organism and the external environment. It prevents loss of body fluids, regulates body temperature, and prevents entry of many substances. However, the skin is a route of entry for some toxicants, especially those that can combine with the lipid portion of the subcutaneous layer of the skin. Dermal toxicants can cause irritation, sensitization, pigmentation changes, chloracne, ulcerations, and cancer.

The skin can also be a major route of entry for other substances, such as pesticides and solvents.

Abrasions, splitting, chafing, cuts, or puncture wounds of the skin break the protective barrier and allow toxic material direct access to underlying tissues and blood vessels, through which it may travel to every part of the body. Compounds that are injected in this way, may

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move rapidly to damage the target organs; example, organophosphate pesticides affect the nervous system. Similarly, compounds that enter by other routes may affect the skin, for example, the ingestion of arsenic causes dermal lesions.

Common toxic reactions to dermal exposures include the following.

- ! Caustic effects such as dermatitis, irritation, rashes, and itching from
  - C acids such as hydrochloric acid, nitric acid, sulfuric acid,
  - C gases such as sulfur dioxide, nitrogen dioxide,
  - C solvents such as acetone, chloroform, toluene, xylene, phenol, and
  - C iodine, mercury.
- ! Allergic reactions such as rash and swelling from
  - C formaldehyde, ammonia, mercury, cobalt, chromates, nitrobenzene, pesticides.
- ! Photosensitizers (sensitivity to light) from
  - C creosotes, pyridine, naphthalene.
- ! Folliculitis or chloracne from
  - C PCB.
- ! Pigmentation changes such as keratosis, ulcers, and cancer from
  - C arsenic compounds, silver compounds.
- ! Systemic reactions via absorption through skin capillaries, including
  - C formate poisoning from formaldehyde,
  - C hypocalcemia from hydrofluoric acid, oxalic acid,
  - C pulmonary edema from paraquat,
  - C hepatitis or liver damage from phosphorus,
  - C seizures, coma, or hepatitis from phenol, and
  - C death from hydrogen cyanide.

3.7.3 SENSORY SYSTEM

The eyes and ears are areas that will be exposed to dangerous chemicals in the air, unless you wear personal protective equipment (PPE) to protect them. The mucus and sebaceous secretions covering these structures serves to lubricate, protect, neutralize, and trap foreign particles. However, many chemicals can penetrate this barrier and be absorbed into the underlying tissues and into the bloodstream.

The conjunctiva and mucous membranes of the eye are very sensitive to many acids, alkalines, solvents, and pesticides. Be careful to avoid:

- ! lacrimators such as tear gas, chloroacetophenone, and MACE that cause

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Ctearing at low concentrations and
Ccornea damage at high concentrations; and

! permanent eye damage or blindness from

Cretina damage from naphthalene, phenothiazine (insecticide),
Ccataract formation from naphthalene, thallium, paradichlorobenzene, and
Coptic nerve damage from thallium, methanol.

A broken ear drum (tympanum) and the sebaceous glands lining the ear may allow toxic chemicals to penetrate causing deafness, ear noises, and headaches.

3.7.4 RESPIRATORY SYSTEM

There are four regions of the respiratory system.

! Nasopharyngeal (nose to pharynx)Clined with cilia and mucus that trap large particles.
! Larynx (vocal cords)Cused to make sounds.
! Tracheobronchial areaClined with cilia and mucus to trap smaller particles and move them up to be expelled by coughing, sneezing, or swallowing.
! Lungs (bronchiole to alveoli)Cwhere the exchange of oxygen and carbon dioxide between the blood and air occurs, microscopic particles are trapped.

When the nose and throat mucous membranes are exposed to toxic chemicals, rhinitis, sinusitis, pharyngitis, headaches, and cancer may develop.

Chemicals that irritate the lungs can lead to discomfort. Although the effects of exposure to irritants are usually reversible, chronic exposure may lead to permanent cell damage. The normal, necessary exchange of gases across lung tissues in the alveoli can be impaired by compounds that constrict the respiratory passages, affect secretions, or physically remain in the lung. Gaseous irritants that are insoluble in water will be trapped in the alveoli and clog the route of gaseous exchange. Substances that cause necrosis (cell death), edema (excessive fluid retention), or fibrosis (change in cell type and composition) will impair lung function. Exposure to some substances, such as cigarette smoke, asbestos, and arsenic, can lead to impaired lung function and cancer. Inhaled toxic chemicals may damage

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specific parts of the respiratory system and cause bronchitis, pulmonary edema, asthma, pneumonitis, pneumonia, fibrosis, or cancer. Toxic material may also pass directly into the bloodstream via the capillaries in the alveoli to damage the liver, kidneys, heart, or brain.

Common toxic reactions to respiratory exposures are as follows.

! Simple asphyxiants displace oxygen to cause headaches, giddiness, nausea, confusion, collapse, hyperventilation, seizures, and death. Simple asphyxiants include nitrogen, carbon dioxide, natural gas, methane, helium, neon, and argon.

! Chemical asphyxiants interfere with oxygen transport to cells and cause the same symptoms as simple asphyxiants. Chemical asphyxiants include cyanide and carbon monoxide (the leading fatal poison in the U.S.). Carbon monoxide binds to the hemoglobin in red blood cells and prevents them from carrying oxygen.

! Gaseous irritants dissolve in water to form acids or bases which damage mucous pathways and cause burning, coughing, wheezing, sore throat, bronchitis, and edema. These irritants include hydrofluoric acid, hydrochloric acid, ammonia, chlorine, phosgene, and nitrogen oxides.

! Hydrocarbon solvent poisoning is caused by lipid-soluble compounds that affect the central nervous system and cause giddiness, euphoria, hallucinations, headache, confusion, drowsiness, cardiac arrhythmias, liver and kidney damage, coma, respiratory arrest, and death. These poisons include: aromatic, aliphatic, and halogenated hydrocarbons, as well as alcohols and insecticides (lindane, DDT, and chlordane).

! Alveolar destructive agents destroy the structure of alveoli, often leading to emphysema, and inhibit carbon dioxide/oxygen exchange. These agents include tobacco smoke, wood and coal smoke, phthalic anhydride, aluminum, cadmium dioxide, nitrous oxide, and ozone.

! Fibrosis producers cause fibrotic lesions in lung tissue. These include: asbestos, silicates, and beryllium.

! Allergens produce allergic reactions, constriction of the bronchia, and shock. Allergens include: isocyanates and sulfur dioxide.

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3.7.5 DIGESTIVE SYSTEM

The functions of the digestive system are to:

- ingest and digest foods for nutrients;
- excrete undigested wastes; and
- absorb nutrients and water through the intestine into the bloodstream to supply the liver, kidney, heart, brain, and all body cells and other organs.

Common toxic substances can cause adverse reactions in the digestive system. Gastrointestinal irritants cause gastroenteritis, and other inflammatory and ulcerative diseases. These irritants include metals (barium, cadmium, arsenic, beryllium, boron, lead, iron, lithium), rodenticides, insecticides, and asbestos.

3.7.6 LIVER, PANCREAS, AND SPLEEN

The functions of the liver, pancreas, and spleen are to:

- filter, detoxify, and stabilize the components of the blood.

The spleen removes old or damaged red blood cells and help maintain the immune system. The liver filters and detoxifies the blood. A major function of the liver is metabolism, that is, the biochemical conversion of one substance into another for purposes of nutrition, storage, detoxification, or excretion. The liver has many mechanisms for each of these processes, and interference with any of them can lead to a toxic effect.

Many chemical toxicants and carcinogens enter the body's blood supply via contaminated food and water. Chemicals that damage the liver are called hepatotoxic chemicals. Toxic damage to the liver can include lipid (fat) accumulation, jaundice, necrosis, cirrhosis, and cancer. Since blood that has absorbed compounds from the gastrointestinal tract passes through the liver before the rest of the body, the liver is a major site for the removal of nutrients and toxicants. Elimination of the absorbed toxicants can occur in the feces via the bile, which is produced by the liver, secreted via the gall bladder to the small intestine, where it aids in the absorption of fats. Thus, an impairment of liver function can affect absorption of compounds. Since the spleen and the liver are sites of destruction of aged red blood cells, jaundice is

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an indicator of malfunction of these organs.

Necrosis, or cell death, can have multiple causes. Toxicants can directly or indirectly destroy cells. The liver has a limited ability to regenerate destroyed cells, but chronic destruction of cells may lead to cirrhosis in which damaged liver cells are replaced by connective tissue cells. Many chemicals, such as vinyl chloride and PCB, have been shown to cause liver cancer in laboratory animals.

Exposures to toxic substances cause the following.

- Liver, pancreas, and spleen toxicity is caused by iron, manganese, selenium, aromatic hydrocarbons (benzene), solvents, degreasers (carbon tetrachloride), halogenated aliphatic hydrocarbons (chloroform), herbicides, insecticides, and pesticides.
- Liver damage and cancer are caused by vinyl chloride, and selenium sulfide following long term exposure.
- Liver damage and necrosis are caused by copper salts.

3.7.7 CARDIOVASCULAR SYSTEM

The cardiovascular system includes the heart, blood, and lymph vessels. For the sake of brevity, the liver, pancreas, and spleen are discussed here also since toxic chemicals are carried to these organs by the bloodstream.

The functions of the cardiovascular system include:

- distributing nutrients and oxygen to all cells; and
- carrying metabolic wastes away from cells to be expelled from the body (such as carbon dioxide expelled from the lungs; urea, other metabolic wastes, and toxic chemicals flushed out through the kidneys in urine).

In humans, blood cells are formed in the bone marrow. The three major types of blood cells are formed from precursor cells in bone marrow. Red blood cells contain hemoglobin and transport oxygen and carbon dioxide. White blood cells function as part of the immune system. Platelets are necessary for blood clotting. Chemicals toxic to bone marrow can affect blood cell formation. Depending on the stage and cell affected, the blood cells may be decreased in number. Abnormal increases in production of certain blood cells are also possible, as in leukemia.

Blood plasma contains a number of proteins, ions, and other compounds. Changes in the chemical composition of blood may indicate a toxic response. Also, some chemicals bind to plasma

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proteins. Changes in plasma protein composition could alter the effective concentration of a toxicant.

The normal function of hemoglobin in red blood cells is critical to the transport of oxygen to and carbon dioxide from all cells in the body. Chemicals can affect hemoglobin by chemically oxidizing the iron in the heme group (causing methemoglobinemia) or by otherwise changing the chemical structure of hemoglobin.

The rate and efficiency of the pumping action of the heart can be altered in many ways and by many chemicals. Some toxic materials also constrict or dilate the blood vessels and thus affect circulation of the blood. Cardiovascular damage may result in shock reactions, arrhythmias (irregular heartbeat), cardiomyopathy (heart muscle damage), and myocardial infarction (blood clots in heart arteries).

Circulatory system exposures to toxic substances cause the following.

- Blood cell and bone marrow damage, including platelet and white blood cell deficiency, loss of clotting ability, and loss of body defenses. Substances that cause these effects include: paint solvents, organic solvents (benzene), lead, refrigerants (freon), propellants, carbon monoxide, and pesticides.
- Red blood cell damage; hemoglobin binders are cyanides, carbon monoxide, and many solvents. Hemolysis is caused by arsenic, naphthalene, and rodenticides (Warfarin).

3.7.8 URINARY OR EXCRETORY SYSTEM

The kidney concentrates wastes for elimination and retains nutrients and water that are useful to the body. The kidney can metabolize and detoxify some of the same compounds as the liver, only the kidney operates more slowly.

Compounds that injure the kidney are called renal toxicants. Some renal toxicants may cause cell death (necrosis) or cancer. Also the kidney produces chemicals necessary for homeostasis (balance of functions), and it responds to the hormonal balance and the nervous system. To efficiently remove the body's waste, the kidneys must process large volumes of blood. Thus, this organ is very susceptible to changes in blood flow, either by blockage (clots or kidney stones) or

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chemicals that constrict or dilate blood vessels.

Excessive elimination of water, salts, or other nutrients can be as harmful as failure to eliminate wastes. The effective dose of toxicants in the kidneys may be higher than that for the rest of the body because the kidneys concentrate some toxicants. Toxicants that cause necrosis can also impair renal function. Failure of the kidneys to filter properly is frequently detected by an increase in wastes in the blood or an increase in nutrients in the urine.

Toxicants that affect the urinary tract cause renal toxicity and kidney malfunction. These toxicants include heavy metals (lead, arsenic, beryllium, cadmium, chromium, mercury), and halogenated aliphatic hydrocarbons such as vinyl chloride, antifreeze (ethylene glycol), other aromatic hydrocarbons (benzene), herbicides, and insecticides.

3.7.9 CENTRAL NERVOUS SYSTEM

The central nervous system consists of the brain and spinal cord. The major function of the central nervous system (CNS) is communication. Control of reflexes, movement, sensory information, autonomic functions such as breathing, and intelligence are controlled by the CNS. These functions can be impaired by toxicants. Damage to the nervous system can occur in the brain or other nerve cells, in nerve processes that extend through the body, in the myelin sheaths that cover these nerves, and at the nerve-nerve or nerve-muscle junctions. Damage to nerve cell functions are often called "neuropathies."

As in other cells, damage to the cell body of a neuron (nerve cell) can result in impaired function or death. The brain is partially protected by the blood-brain barrier, which blocks or reduces the passage of some substances to the brain; however, some chemicals, such as organic mercury, tend to concentrate in the brain.

Toxic effects on the CNS may be difficult to detect in a person's behavior, but exposure to some chemicals can cause headaches, fatigue, or irritability. Although these symptoms are mild and difficult to assess, they are frequently an early warning of exposure to a toxicant.

Toxic damage to the CNS may result in seizures, neuropathies, coma, psychological or personality or mood changes, impaired thinking ability, and dementia (mental impairment).

Toxicants affecting the CNS can cause the following.

- CNS depression; its symptoms are decreased alertness, headache, sleepiness, loss of consciousness. This can be caused by exposure to aromatic hydrocarbon solvents

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(benzene, toluene, and xylene), and halogenated hydrocarbons (carbon tetrachloride, chloroform, TCE, and vinyl chloride).

! CNS malfunction; its effects are decreased mental ability and brain damage. This can be caused by lead poisoning, and exposure to other heavy metals. One symptom of CNS malfunction is numbness. Another effect, long-term nerve damage, can result from exposure to insecticides and herbicides.

3.7.10 REPRODUCTIVE SYSTEM

Reproductive toxicology involves the damage caused to male and female parents and their offspring. Toxic effects include an impaired ability to conceive, the failure of the fetus to survive, and the production of abnormal offspring.

Problems with conception usually result from impaired production of sperm or egg. Sperm production is continuous in the male, so any chemical that interferes with the development or maturation of the sperm may prevent sperm production, cause sterility, reduce sperm production, or produce abnormal sperm with a reduced capacity to fertilize. Likewise, any chemical that interferes with egg production (usually one per month), or proper maturation of the egg may interfere with conception and the development of a normal fetus. A "mutagenic" agent is one that causes a change in the genetic (DNA) structure of the fertilizing sperm or egg, causing lethal, severe, or mild damage. Death of the fetus, whether at the early embryonic stage or later fetal stage, can be caused by a variety of factors including chemicals. Such chemicals are labeled "embryo-toxic" and "feto-toxic," respectively.

Teratogens are chemicals that cause defects in fetal development and result in abnormal offspring. The defects may range from abnormal skeletal or muscle structure and mental retardation, to metabolic malfunctions, to subtle malfunctions that may not be noticed during a normal life.

Although the placenta is a good barrier, many chemicals have been found to cross to the embryo. Depending on the compound, the final concentration may be higher in the mother, higher in the embryo, or equal in both. Moreover, the placenta is not inert but is capable of metabolizing some chemicals into toxic substances.

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The timing of exposure is important in teratogenesis. Time of exposure to the potential teratogen may not only determine which developing system is affected but also whether the compound will have any effect at all. For each developing system there is a critical period, usually between three and twelve weeks in the human, during which the system is particularly sensitive to chemical toxicants. Although damage may occur after this period, the abnormalities are usually less severe.

Toxicants that affect the reproductive system are noted below.

- Reproductive toxicants that cause sterility, or lower fertility. These toxicants include metals, chlorinated organics and anesthetics.
- Mutagens that cause irreversible DNA changes. Mutagens include mercury, lead compounds, benzopyrene, mustard gas, hydrazine (rocket fuel), hydrogen peroxide, ethylene oxide, ultraviolet light, and X-rays.
- Teratogenic substances that damage any system in the embryo. These substances include methyl mercury, lead compounds, alcohol, diethylstilbestrol (DES), thalidomide, insecticides, pesticides, solvent, and X-rays.

3.8 EXPOSURE PREVENTION TECHNIQUES

When you are in any area that may be hazardous to your life or health, you are obligated to know and understand the following techniques for preventing exposure:

- know the toxicity of the materials,
- know the standard operating procedures for each situation,
- don personal protective equipment properly,
- know the engineering controls available,
- know proper personal hygiene (where to eat and drink safely), and
- use your common sense and intuition.

By using these precautions, you can control exposures, keep a dose at safe limits, prevent toxic effects, and handle any material safely.

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3.9 ADDITIONAL READING

NIOSH. *Pocket Guide to Chemical Hazards*. U.S. Dept. of Health and Human Services, Public Health Services, Centers for Disease Control, National Institute for Occupational Safety and Health. Atlanta, GA.

Gosselin, R.E., et. al. *Clinical Toxicology of Commercial Products*. Williams and Wilkins, Baltimore, MD.

Casarett and Doull's *Toxicology*. Macmillan Publishing Company, New York.

Lu, F.C. *Basic Toxicology*. Taylor & Francis Publishing, Bristol, PA.